Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:54:37 ON 25 MAY 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:54:47 ON 25 MAY 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 MAY 2007 HIGHEST RN 935837-89-1
DICTIONARY FILE UPDATES: 24 MAY 2007 HIGHEST RN 935837-89-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

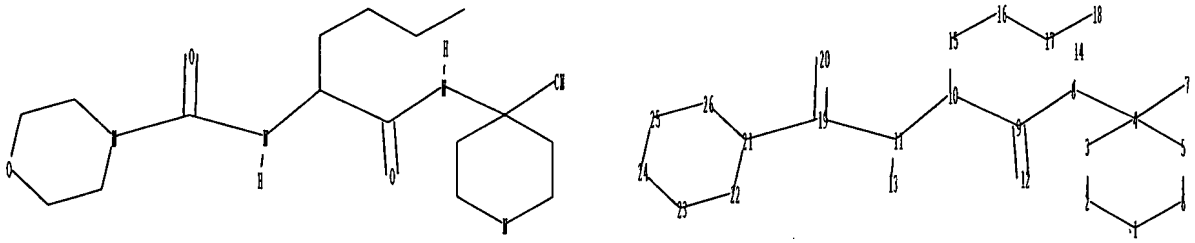
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10790549.str



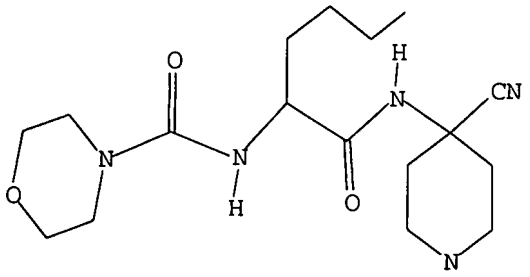
chain nodes :
7 8 9 10 11 12 13 14 15 16 17 18 19 20
ring nodes :
1 2 3 4 5 6 21 22 23 24 25 26
chain bonds :
4-7 4-8 8-9 8-14 9-10 9-12 10-11 10-15 11-13 11-19 15-16 16-17 17-18 19-20 19-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 21-22 21-26 22-23 23-24 24-25 25-26

exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 4-8 5-6 8-9 9-12 10-11 11-19 19-20 19-21 21-22
21-26 22-23 23-24 24-25 25-26
exact bonds :
4-7 8-14 9-10 10-15 11-13 15-16 16-17 17-18

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 13:55:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 228 TO ITERATE

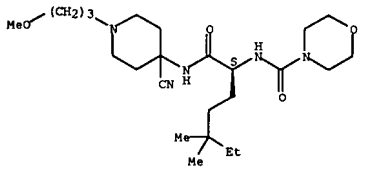
100.0% PROCESSED 228 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

L2 8 SEA SSS FUL L1

=> d l2 1-8

L2 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN
RN 864971-57-3 REGISTRY
ED Entered STN: 11 Oct 2005
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(3-methoxypropyl)-4-piperidinyl]amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H43 N5 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

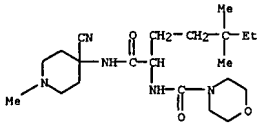
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

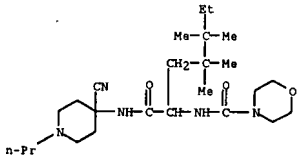
L2 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-79-9 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
MF C21 H37 N5 O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-77-7 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylhexyl]- (9CI) (CA INDEX NAME)
MF C25 H45 N5 O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

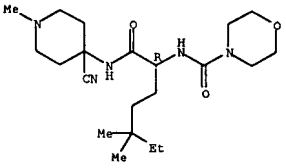


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-75-5 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H37 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

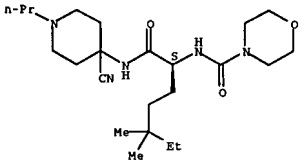


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-70-0 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H41 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

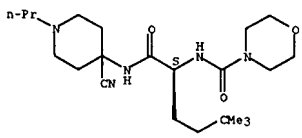


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-69-7 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H39 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

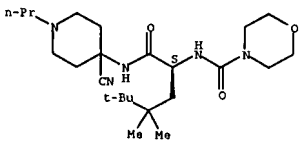


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-68-6 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H43 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

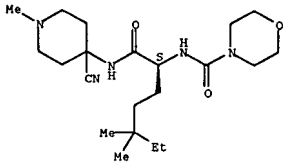


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-67-5 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H37 N5 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

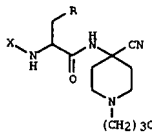
L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1078240 CAPLUS
DOCUMENT NUMBER: 143:306552
TITLE: Preparation of 4-piperidinecarbonitrile peptidyl compounds as cathepsin S inhibitors
INVENTOR(S): Hickey, Eugene R.; Liu, Wiemen; Sun, Sanxing; Ward, Yancey David; Young, Erick Richard Roush
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 790,549.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005222145	A1	20051006	US 2005-141153	20050531
US 2004180886	A1	20040916	US 2004-790549	20040301
AU 2004221860	A1	20040930	AU 2004-221860	20040303
CA 2518728	A1	20040930	CA 2004-2518728	20040303
EP 1606258	A1	20051221	EP 2004-716966	20040303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008299	A	20060307	BR 2004-8299	20040303
JP 2006519768	T	20060831	JP 2005-518890	20040303

PRIORITY APPLN. INFO.: US 2003-454239P P 20030313
US 2004-790549 A2 20040301
WO 2004-US6554 W 20040303

OTHER SOURCE(S): MARPAT 143:306552
GI



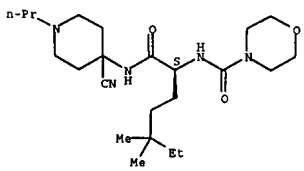
(CH2)3OMe I

AB The invention relates to peptidyl compds. I [R is CH2CMe2Et or CMe2CMe3; X is 4-morpholinecarbonyl, (7-fluoro)-2-oxobenzo[e][1,3]oxazin-4-yl, 2-oxobenzo[e]pyrimidin-4-yl, 1,1-dioxobenzo[d][1,2]thiazol-3-yl] or their pharmaceutically-acceptable salts, which are reversible inhibitors of cathepsin S and therefore useful in the treatment of autoimmune and other diseases. Thus, peptide I (R = CH2CMe2Et, X = 4-morpholinecarbonyl) was prepared by coupling reaction of (S)-5,5-dimethyl-2-[(4-morpholinecarbonyl)amino]heptanoic acid with 4-amino-1-(3-methoxypropyl)-4-piperidinecarbonitrile.

IT 752237-67-5P 752237-68-6P 752237-69-7P
752237-70-0P 752237-75-5P 752237-79-9P
864971-57-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

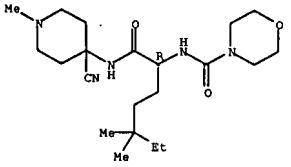
L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.

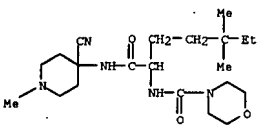


RN 752237-75-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 752237-79-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)



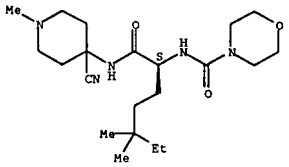
RN 864971-57-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(3-methoxypropyl)-4-piperidinyl]amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(prepn. of piperidinecarbonitrile peptidyl compds. as cathepsin S inhibitors)

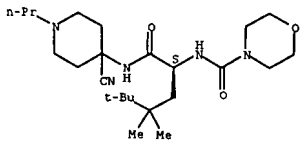
RN 752237-67-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



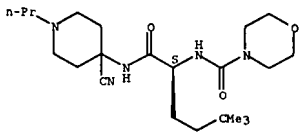
RN 752237-68-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



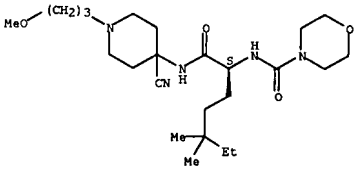
RN 752237-69-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 752237-70-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:564583 CAPLUS
DOCUMENT NUMBER: 143:71764
TITLE: Use of cathepsin s inhibitors for treating an immune response caused by administration of a small molecule therapeutic or biologic
INVENTOR(S): Elrod, Kyle C.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058348	A1	20050630	WO 2004-US41580	20041210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1694357	A1	20060830	EP 2004-813839	20041210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				

PRIORITY APPLN. INFO.:	US 2003-528846P	P	20031211
	US 2003-532202P	P	20031223
	WO 2004-US41580	W	20041210

OTHER SOURCE(S): MARPAT 143:71764

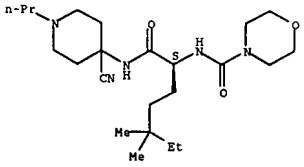
AB The present invention is directed to the use of Cathepsin S inhibitors in combination with a therapy that causes a deleterious immune response in patients receiving the therapy.

IT 752237-67-5 752237-68-6 752237-69-7
752237-70-0 752237-75-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cathepsin S inhibitors for treating an immune response caused by administration of a small mol. therapeutic or biol.)

RN 752237-67-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

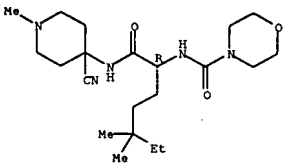
Absolute stereochemistry.

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



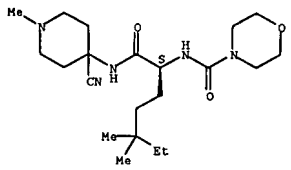
RN 752237-75-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



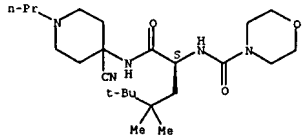
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



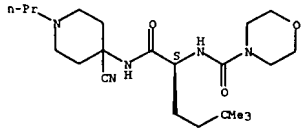
RN 752237-68-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 752237-69-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 752237-70-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:429398 CAPLUS
DOCUMENT NUMBER: 142:464024
TITLE: Synthesis of dipeptide analogue
INVENTOR(S): Busacca, Carl Alan; Haddad, Nizar; Kapadia, Suresh R.; Smith Keenan, Lana; Lorenz, Jon Charles; Senanayake, Chris Hugh; Wei, Xudong
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005044799	A1	20050519	WO 2004-US35833	20041027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2543884	A1	20050519	CA 2004-2543884	20041027
US 2005113572	A1	20050526	US 2004-976094	20041027
US 7186827	B2	20070306		
EP 1682506	A1	20060726	EP 2004-816314	20041027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007509961	T	20070419	JP 2006-538254	20041027

PRIORITY APPLN. INFO.:	US 2003-515848P	P	20031030
	WO 2004-US35833	W	20041027

OTHER SOURCE(S): CASREACT 142:464024; MARPAT 142:464024

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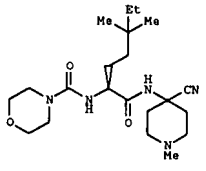


I

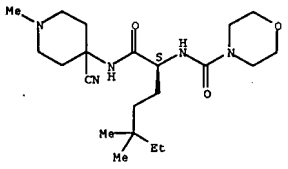
AB The invention discloses a process for making dipeptide compds. R2NCONHCH(CH2CH2CR1R2Et)CONHCR'2R3 [R2N is a mono- or bicyclic heterocyclic or heteroaryl ring; CR'2 is a ring (azepanyl, piperidinyl, pyrrolidinyl, azetidinyl, oxepanyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrofuranyl, oxetanyl, etc.); R1, R2 are

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
independently alkyl, alkoxy, carbocyclyl, carbocyclyl-S(O)0-2, alkyl-S(O)0-2, heterocyclyl or heteroaryl; R3 is cyano, amino or -CO-Ar, where Ar is heterocyclyl, heteroaryl or carbocyclyl]. The process involves reaction of an allyl alc. R1R2C:CHCH2OH with a vinyl ether CH2:CH(OCH2CH2)2-5OCH:CH2 in the presence of a palladium catalyst and a ligand to form an aldehyde CH2:CHCR1R2CH2CHO. The latter underwent Horner-Emmons-Wadsworth reaction with phosphonate intermediate R2NCONHCH[P(O)(OMe)2]CO2Me, obtained from PhCH2O2CNHCH[P(O)(OMe)2]CO2Me by catalytic hydrogenation and reaction with R2NCO-X. Subsequent asym. catalytic hydrogenation, hydrolysis, and reaction with H2NCR'2R3 afforded the desired product. The method was applied to the synthesis of dipeptide I.

IT 752237-67-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of dipeptide analog)

RN 752237-67-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:759825 CAPLUS
DOCUMENT NUMBER: 141:243834
TITLE: Preparation of 4-piperidinecarbonitrile peptidyl compounds as cathepsin S inhibitors
INVENTOR(S): Hickey, Eugene R.; Liu, Wiemen; Sun, Sanxing; Ward, Yancey David; Young, Erick Richard Roush
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180886	A1	20040916	US 2004-790549	20040301
AU 2004221860	A1	20040930	AU 2004-221860	20040303
CA 2518728	A1	20040930	CA 2004-2518728	20040303
WO 2004083182	A1	20040930	WO 2004-US6554	20040303
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1606258	A1	20051221	EP 2004-716966	20040303
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK			
BR 2004008299	A	20060307	BR 2004-8299	20040303
CN 1761652	A	20060419	CN 2004-80006887	20040303
JP 2006519768	T	20060831	JP 2005-518890	20040303
US 2005222145	A1	20051006	US 2005-141153	20050531
PRIORITY APPLN. INFO.:			US 2003-454239P P	20030313
			US 2004-790549 A2	20040301
			WO 2004-US6554 W	20040303

OTHER SOURCE(S): MARPAT 141:243834
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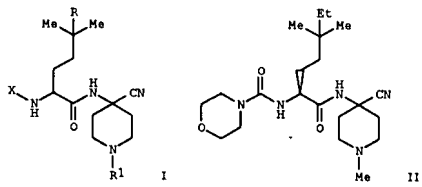


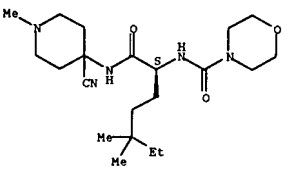
L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB The invention relates to peptidyl compds. I [R is Me or Et; R1 is H, (un)substituted alkyl or heteroalkyl, where hetero signifies O, S, NH or alkylimino; X is (7-fluoro)-2-oxobenzo[e][1,3]oxazin-4-yl, 2-oxobenzo[e]pyrimidin-4-yl, 1,1-dioxobenzo[d][1,2]thiazol-3-yl] or their pharmaceutically-acceptable salts, which are reversible inhibitors of cathepsin S and therefore useful in the treatment of autoimmune and other diseases. Thus, peptide II was prepared by coupling reactions of (S)-2-(tert-butoxycarbonylamino)-5,5-dimethylheptanoic acid, 4-amino-1-methyl-4-piperidinecarbonitrile, and 4-morpholinecarbonyl chloride.

IT 752237-67-5P 752237-68-6P 752237-69-7P
752237-70-0P 752237-75-5P 752237-77-7P
752237-79-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinecarbonitrile peptidyl compds. as cathepsin S inhibitors)

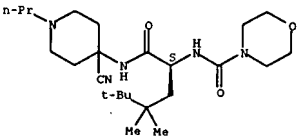
RN 752237-67-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 752237-68-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl]- (9CI) (CA INDEX NAME)

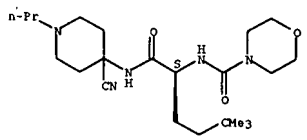
Absolute stereochemistry.



RN 752237-69-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl]- (9CI) (CA INDEX NAME)

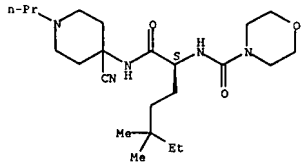
L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



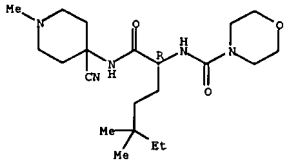
RN 752237-70-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

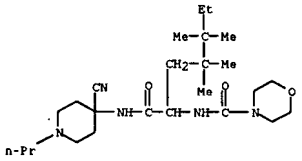


RN 752237-75-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

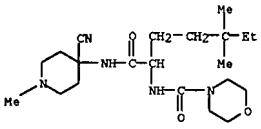
Absolute stereochemistry.



RN 752237-77-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylhexyl]- (9CI) (CA INDEX NAME)



RN 752237-79-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	24.84	214.10

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.12	-3.12

FILE 'REGISTRY' ENTERED AT 14:02:05 ON 25 MAY 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 MAY 2007 HIGHEST RN 935837-89-1
DICTIONARY FILE UPDATES: 24 MAY 2007 HIGHEST RN 935837-89-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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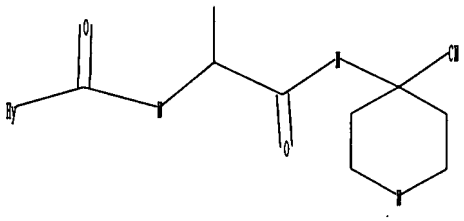

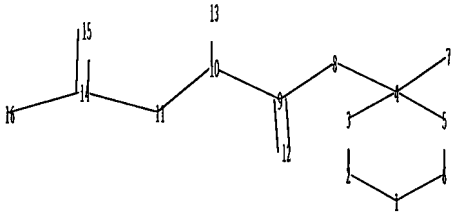

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ring nodes :
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ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
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exact bonds :
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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
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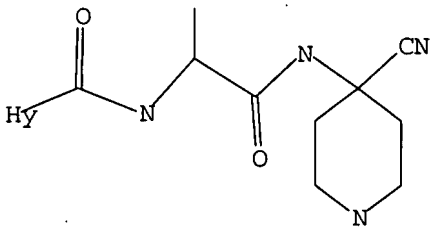

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FULL SCREEN SEARCH COMPLETED - 797 TO ITERATE

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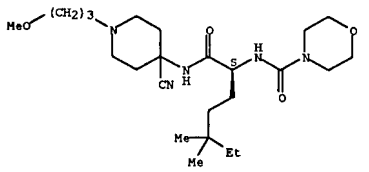
L5 ANSWER 1 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 864971-57-3 REGISTRY
ED Entered STN: 11 Oct 2005
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(3-methoxypropyl)-4-piperidinyl]amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H43 N5 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

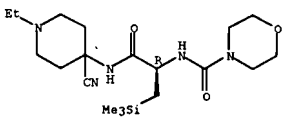


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 2 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 862693-52-5 REGISTRY
ED Entered STN: 08 Sep 2005
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(4-cyano-1-ethyl-4-piperidinyl)amino]-2-oxo-1-[(trimethylsilyl)methyl]ethyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Morpholine-4-carboxylic acid [(1R)-1-[(4-cyano-1-ethylpiperidin-4-yl)carbamoyl]-2-(trimethylsilanyl)ethyl]amide
FS STEREOSEARCH
MF C19 H35 N5 O3 Si
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

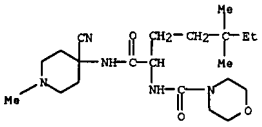
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 3 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-79-9 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
MF C21 H37 N5 O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 4 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-77-7 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylhexyl]- (9CI) (CA INDEX NAME)
MF C25 H45 N5 O3
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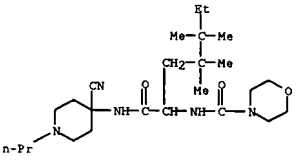
LC STN Files: CA, CAPLUS, USPATFULL

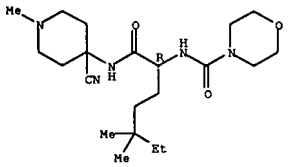


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 5 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-75-5 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H37 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



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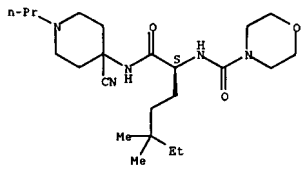
3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 6 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-70-0 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H41 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

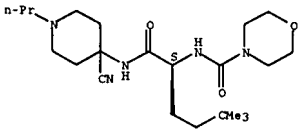


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 7 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-69-7 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H39 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

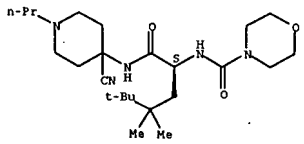


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 8 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-68-6 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H43 N5 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

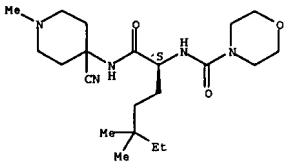


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 9 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 752237-67-5 REGISTRY
ED Entered STN: 27 Sep 2004
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H37 N5 O3
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

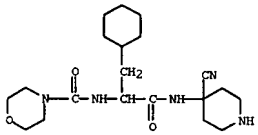
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 10 OF 77 REGISTRY COPYRIGHT 2007 ACS on STN
RN 747400-12-0 REGISTRY
ED Entered STN: 19 Sep 2004
CN 4-Morpholinecarboxamide, N-[2-[(4-cyano-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)
MF C20 H33 N5 O3
CI COM
SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

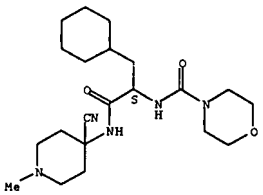
L6 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:488391 CAPLUS
DOCUMENT NUMBER: 145:159375
TITLE: An orally active reversible inhibitor of cathepsin S inhibits human trans vivo delayed-type hypersensitivity
AUTHOR(S): Desai, Sudha N.; White, Della M.; O'Shea, Kathryn M.; Brown, Maryanne L.; Cywin, Charles L.; Spero, Denice M.; Panzenbeck, Maret J.
CORPORATE SOURCE: Department of Immunology and Inflammation, Boehringer Ingelheim Pharmaceutical Inc., Ridgefield, CT, 06877-0368, USA
SOURCE: European Journal of Pharmacology (2006), 538(1-3), 168-174
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cathepsin S is a major histocompatibility complex (MHC) class II associated invariant chain (Ii) degrading enzyme expressed in antigen presenting cells such as B cells and dendritic cells. This enzyme is essential for MHC class II associated antigen processing and presentation to CD4+ T cells. Compound I, a selective, reversible and orally bioavailable, inhibitor of cathepsin S, with mol. IC50 = 9 nM, has been recently described. We have tested the effects of compound I in a trans vivo model of delayed-type hypersensitivity. Human peripheral blood mononuclear cells (7-10 + 106) from tetanus-sensitized donors were co-injected with tetanus toxoid (0.25 Lf) into C57Bl/6 mouse footpads. At 24 h, significant footpad swelling (+ 0.024 ± 0.001 cm) characterized by an influx of mouse neutrophils and monocytes was observed Injection of peripheral blood mononuclear cells alone caused negligible swelling (0.002 ± 0.0002 cm). Anti-human MHC class II (HLA-DR, DP, DQ) antibody (5 mg/kg, i.p.) inhibited the swelling 91 ± 7%, thus demonstrating a role of human antigen presenting cells in this model. Compound I (10, 30, and 100 mg/kg, p.o.) inhibited the response with an ED50 of .apprx.10 mg/kg. Compound III, a less active analog (mol. IC50 > 20 μM) had no effect. Furthermore, pretreatment of peripheral blood mononuclear cells with 10 nM compound II, an irreversible inhibitor (mol. IC50 = 11 nM) inhibited swelling 87 ± 4%. These findings support the role of cathepsin S in human delayed-type hypersensitivity. Inhibition of cathepsin S with compound I may be useful in the treatment of human autoimmune diseases like rheumatoid arthritis and multiple sclerosis.

IT 331278-68-3
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of reversible inhibitor of cathepsin S in delayed-type hypersensitivity)
RN 331278-68-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

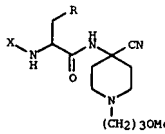


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1078240 CAPLUS
DOCUMENT NUMBER: 143:306552
TITLE: Preparation of 4-piperidinecarbonitrile peptidyl compounds as cathepsin S inhibitors
INVENTOR(S): Hickey, Eugene R.; Liu, Wiemen; Sun, Sanxing; Ward, Yancey David; Young, Erick Richard Roush
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 790,549.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005222145	A1	20051006	US 2005-141153	20050531
US 2004180886	A1	20040916	US 2004-790549	20040301
AU 2004221860	A1	20040930	AU 2004-221860	20040303
CA 2518728	A1	20040930	CA 2004-2518728	20040303
EP 1606258	A1	20051221	EP 2004-716966	20040303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008299	A	20060307	BR 2004-8299	20040303
JP 2006519768	T	20060831	JP 2005-518890	20040303
PRIORITY APPLN. INFO.:			US 2003-454239P P	20030313
			US 2004-790549 A2	20040301
			WO 2004-US6554 W	20040303

OTHER SOURCE(S): MARPAT 143:306552
GI



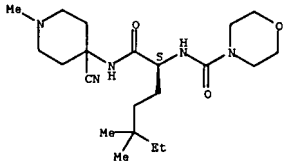
(CH2)3OMe I

AB The invention relates to peptidyl compds. I [R is CH2CMe2Et or CMe2CMe3; X is 4-morpholinecarbonyl, (7-fluoro)-2-oxobenzo[e][1,3]oxazin-4-yl, 2-oxobenzo[e]pyrimidin-4-yl, 1,1-dioxobenzo[d][1,2]thiazol-3-yl] or their pharmaceutically-acceptable salts, which are reversible inhibitors of cathepsin S and therefore useful in the treatment of autoimmune and other diseases. Thus, peptide I (R = CH2CMe2Et, X = 4-morpholinecarbonyl) was prepared by coupling reaction of (S)-5,5-dimethyl-2-[(4-morpholinecarbonyl)amino]heptanoic acid with 4-amino-1-(3-methoxypropyl)-4-piperidinecarbonitrile.

IT 752237-67-5P 752237-68-6P 752237-69-7P
752237-70-0P 752237-75-5P 752237-79-9P
864971-57-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

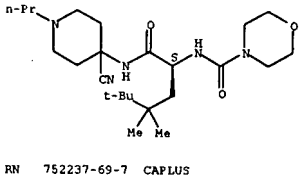
L6 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidinecarbonitrile peptidyl compds. as cathepsin S inhibitors)
RN 752237-67-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



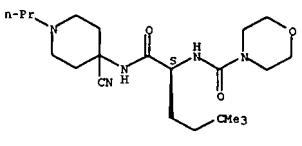
RN 752237-68-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 752237-69-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl]- (9CI) (CA INDEX NAME)

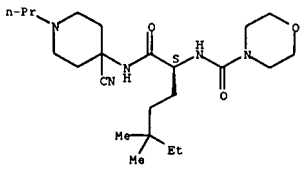
Absolute stereochemistry.



RN 752237-70-0 CAPLUS

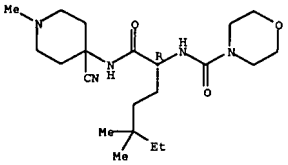
L6 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

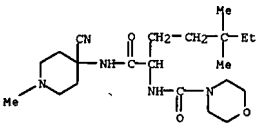


RN 752237-75-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



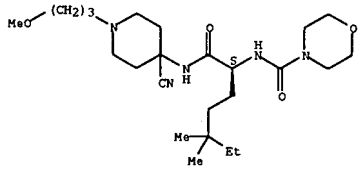
RN 752237-79-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)



RN 864971-57-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(3-methoxypropyl)-4-piperidinyl]amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



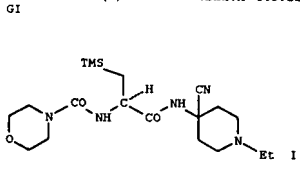
L6 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:811667 CAPLUS
DOCUMENT NUMBER: 143:229992
TITLE: Preparation of silyl-containing carboxamides as cysteine protease inhibitors
INVENTOR(S): Link, John O.; Graupe, Michael
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005074904	A2	20050818	WO 2005-US2773	20050131
WO 2005074904	A3	20050929		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005210631	A1	20050818	AU 2005-210631	20050131
CA 2554626	A1	20050818	CA 2005-2554626	20050131
EP 1716158	A2	20061102	EP 2005-722609	20050131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
BR 2005006494	A	20070213	BR 2005-6494	20050131
CN 1938323	A	20070328	CN 2005-80010399	20050131
NO 2006003842	A	20061020	NO 2006-3842	20060829
US 2007088001	A1	20070419	US 2006-587867	20061221

PRIORITY APPLN. INFO.:		
US 2004-540581P	P	20040130
US 2004-547498P	P	20040224
WO 2005-US2773	W	20050131

OTHER SOURCE(S): MARPAT 143:229992
GI



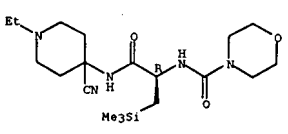
AB The present invention is directed to silyl-containing carboxamides (R3-Q-N(R2)-C(R1)(R1a)-C(O)-N(H)-E (I); variables defined below; e.g. morpholine-4-carboxylic acid [(1R)-1-[(4-cyano-1-ethylpiperidin-4-yl)carbamoyl]-2-(trimethylsilanyl)ethyl]amide (shown as II)) that are

L6 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
inhibitors of cysteine proteases, in particular, cathepsins B, K, L, F, and S and are therefore useful in treating diseases mediated by these proteases. The present invention is also directed to pharmaceutical compns. comprising these compds. and processes for prepg. them. The present invention is also directed to the use of these inhibitors in combination with a therapy that causes a deleterious immune response in patients receiving the therapy. Although the methods of prepn. are not claimed, 11 example prepns. of I are included. For example, II was prepd. in 2 steps starting with amide formation between (R)-2-amino-3-(trimethylsilanyl)propionic acid and morpholinocarbonyl chloride using MSTFA to give 2-(R)-[[(morpholin-4-yl)carbonyl]amino]-3-(trimethylsilanyl)propionic acid which underwent amide formation with 4-amino-4-cyano-1-ethylpiperidine hydrochloride in the presence of HATU and iPr2EtN in DMF. For I: Q is -CO-, -SO2-, -OCO-, -NR4CO-, -NR4SO2-, or -CHR- where R is haloalkyl and R4 is H, alkyl, hydroxyalkyl, alkoxyalkyl, or aralkyl; E is -C(R5)(R6)X1 (X1 is -C(R7)(R8)R10, -CH:CHS(O)2R10, -C(R7)(R8)C(R7)(R8)OR10, -C(R7)(R8)CH2OR10, -C(R7)(R8)CH2N(R11)SO2R10, -C(R7)(R8)C(O)N(R11)(CH2)2OR11, -C(R7)(R8)C(O)NR10R11 or -C(R7)(R8)C(O)N(R11)(CH2)2NR10R11) or -C(R5a)(R6a)CN. R1 is H or alkyl; R1a is 1,1-dialkylsilinan-4-ylalkylene or -(alkylene)-SiR32R33R34 where R32 is alkyl, R33 is alkyl, and R34 is alkyl, alkenyl, cycloalkylalkyl, aryl, aralkyl, heteroaralkyl, or heterocycloalkylalkyl or R33 and R34 together with Si form a heterocycloalkylene ring contg. the Si atom and 3 to 7 C ring atoms wherein one or two C ring atoms are optionally independently replaced with -NH-, -O-, -S-, -SO-, -SO2-, -CO-, -CONH-, or -SO2NH-. R2 is H or alkyl; R3 is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, heterocycloalkylalkyl, or -alkylene-X6-R35 [wherein X6 is -NR36-, -O-, -S(O)n4-, -CO-, -COO-, -OCO-, -NR36CO-, -CONR36-, -NR36SO2-, -SO2NR36-, -NR36COO-, -OCONR36-, NR36CONR37- or NR36SO2NR37- (each R36 and R37 = H, alkyl, or acyl and n4 = 0-2) and R35 is H, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heterocycloalkylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl]; addnl. details are given in the claims.

IT 862693-52-5P, Morpholine-4-carboxylic acid [(1R)-1-[(4-cyano-1-ethylpiperidin-4-yl)carbamoyl]-2-(trimethylsilanyl)ethyl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of silyl-containing carboxamides as cysteine protease inhibitors)

RN 862693-52-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(4-cyano-1-ethyl-4-piperidinyl)amino]-2-oxo-1-[(trimethylsilyl)methyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:564583 CAPLUS
DOCUMENT NUMBER: 143:71764
TITLE: Use of cathepsin s inhibitors for treating an immune response caused by administration of a small molecule therapeutic or biologic
INVENTOR(S): Elrod, Kyle C.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058348	A1	20050630	WO 2004-US41580	20041210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1694357	A1	20060830	EP 2004-813839	20041210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				

PRIORITY APPLN. INFO.: US 2003-528846P P 20031211
US 2003-532202P P 20031223
WO 2004-US41580 W 20041210
OTHER SOURCE(S): MARPAT 143:71764

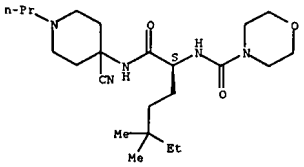
AB The present invention is directed to the use of Cathepsin S inhibitors in combination with a therapy that causes a deleterious immune response in patients receiving the therapy.

IT 752237-67-5 752237-68-6 752237-69-7
752237-70-0 752237-75-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cathepsin S inhibitors for treating an immune response caused by administration of a small mol. therapeutic or biol.)

RN 752237-67-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

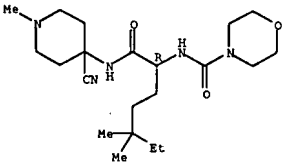
Absolute stereochemistry.

L6 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



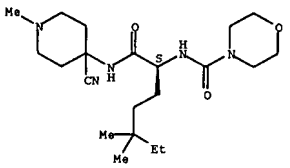
RN 752237-75-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



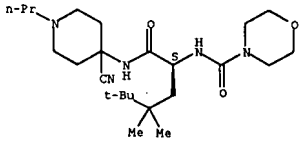
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



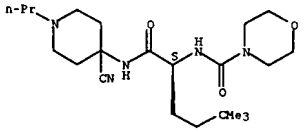
RN 752237-68-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 752237-69-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 752237-70-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

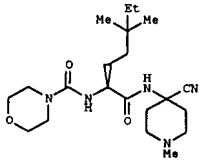
Absolute stereochemistry.

L6 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:429398 CAPLUS
DOCUMENT NUMBER: 142:464024
TITLE: Synthesis of dipeptide analogue
INVENTOR(S): Busacca, Carl Alan; Haddad, Nizar; Kapadia, Suresh R.; Smith Keenan, Lana; Lorenz, Jon Charles; Senanayake, Chris Hugh; Wei, Xudong
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005044799	A1	20050519	WO 2004-US35833	20041027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2543884	A1	20050519	CA 2004-2543884	20041027
US 2005113572	A1	20050526	US 2004-976094	20041027
US 7186827	B2	20070306		
EP 1682506	A1	20060726	EP 2004-818314	20041027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2007509961	T	20070419	JP 2006-538254	20041027

PRIORITY APPLN. INFO.: US 2003-515848P P 20031030
WO 2004-US35833 W 20041027
OTHER SOURCE(S): CASREACT 142:464024; MARPAT 142:464024
GI



AB The invention discloses a process for making dipeptide compds. R2NCONHCH(CH2CH2CR1R2Et)CONHCR'2R3 (R2N is a mono- or bicyclic heterocyclic or heteroaryl ring; CR'2 is a ring (azepanyl, piperidinyl, pyrrolidinyl, azetidinyl, oxepanyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrofuranyl, oxetanyl, etc.); R1, R2 are

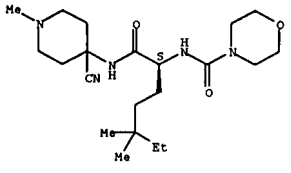
L6 ANSWER 5 OF 10 *CAPLUS COPYRIGHT 2007* ACS on STN (Continued)
independently alkyl, alkoxy, carbocyclyl, carbocyclyl-S(O)0-2, alkyl-S(O)0-2, heterocyclyl or heteroaryl; R3 is cyano, amino or -CO-Ar, where Ar is heterocyclyl, heteroaryl or carbocyclyl]. The process involves reaction of an allyl alc. R1R2C:CHCH2OH with a vinyl ether CH2:CH(OCH2CH2)2-5OCH:CH2 in the presence of a palladium catalyst and a ligand to form an aldehyde CH2:CHCR1R2CH2CHO. The latter underwent Horner-Emmons-Wadsworth reaction with phosphonate intermediate R2NCONHCH[P(O)(OMe)2]CO2Me, obtained from PhCH2O2CNHCH[P(O)(OMe)2]CO2Me by catalytic hydrogenation and reaction with R2NCO-X. Subsequent asym. catalytic hydrogenation, hydrolysis, and reaction with H2NCR'2R3 afforded the desired product. The method was applied to the synthesis of dipeptide I.

IT 752237-67-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of dipeptide analog)

RN 752237-67-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



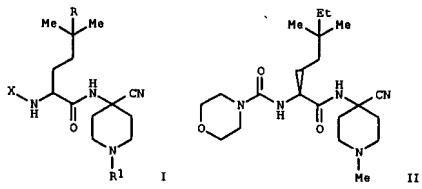
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:759825 CAPLUS
DOCUMENT NUMBER: 141:243834
TITLE: Preparation of 4-piperidinecarbonitrile peptidyl compounds as cathepsin S inhibitors
INVENTOR(S): Hickey, Eugene R.; Liu, Wiemen; Sun, Sanxing; Ward, Yancey David; Young, Erick Richard Roush
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180886	A1	20040916	US 2004-790549	20040301
AU 2004221860	A1	20040930	AU 2004-221860	20040303
CA 2518728	A1	20040930	CA 2004-2518728	20040303
WO 2004083182	A1	20040930	WO 2004-US6554	20040303
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1606258	A1	20051221	EP 2004-716966	20040303
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008299	A	20060307	BR 2004-8299	20040303
CN 1761652	A	20060419	CN 2004-80006887	20040303
JP 2006519768	T	20060831	JP 2005-518890	20040303
US 2005222145	A1	20051006	US 2005-141153	20050531
PRIORITY APPLN. INFO.:			US 2003-454239P	P 20030313
			US 2004-790549	A2 20040301
			WO 2004-US6554	W 20040303

OTHER SOURCE(S): MARPAT 141:243834
GI



I II

L6 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

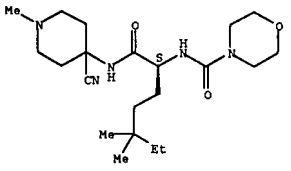
AB The invention relates to peptidyl compds. I [R is Me or Et; R1 is H, (un)substituted alkyl or heteroalkyl, where hetero signifies O, S, NH or alkylimino; X is (7-fluoro)-2-oxobenzo[e][1,3]oxazin-4-yl, 2-oxobenzo[e]pyrimidin-4-yl, 1,1-dioxobenzo[d][1,2]thiazol-3-yl] or their pharmaceutically-acceptable salts, which are reversible inhibitors of cathepsin S and therefore useful in the treatment of autoimmune and other diseases. Thus, peptide II was prepared by coupling reactions of (S)-2-(tert-butoxycarbonylamino)-5,5-dimethylheptanoic acid, 4-amino-1-methyl-4-piperidinecarbonitrile, and 4-morpholinecarbonyl chloride.

IT 752237-67-5P 752237-68-6P 752237-69-7P
752237-70-0P 752237-75-5P 752237-77-7P
752237-79-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinecarbonitrile peptidyl compds. as cathepsin S inhibitors)

RN 752237-67-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

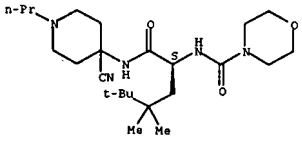
Absolute stereochemistry.



RN 752237-68-6 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

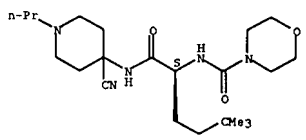


RN 752237-69-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylpentyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

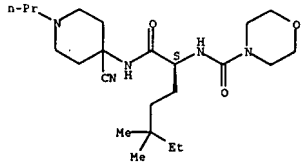
Absolute stereochemistry.



RN 752237-70-0 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

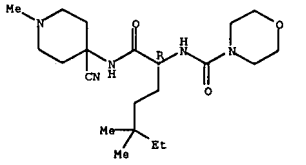
Absolute stereochemistry.



RN 752237-75-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1R)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)

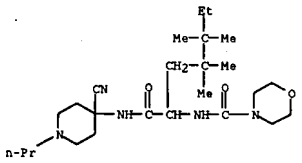
Absolute stereochemistry.



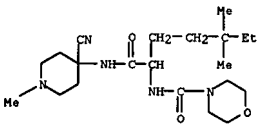
RN 752237-77-7 CAPLUS

CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3,4,4-tetramethylhexyl]- (9CI) (CA INDEX NAME)

L6 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 752237-79-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-4,4-dimethylhexyl]- (9CI) (CA INDEX NAME)



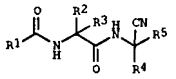
L6 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:515539 CAPLUS
DOCUMENT NUMBER: 141:71829
TITLE: Cyanomethyl derivatives as cysteine protease inhibitors
INVENTOR(S): Graupe, Michael; Lau, Agnes J.; Link, John O.; Liu, Yang; Mossman, Craig J.; Patterson, John W.; Zipfel, Sheila M.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052921	A1	20040624	WO 2003-US37979	20031126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506114	A1	20040624	CA 2003-2506114	20031126
AU 2003298740	A1	20040630	AU 2003-298740	20031126
EP 1569954	A1	20050907	EP 2003-796499	20031126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006122184	A1	20060608	US 2005-536889	20051017
PRIORITY APPLN. INFO.:			US 2002-431354P P	20021205
			WO 2003-US37979 W	20031126

OTHER SOURCE(S): MARPAT 141:71829
GI

L6 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



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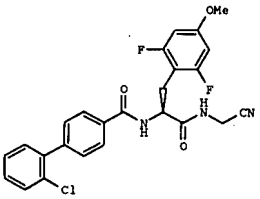


II

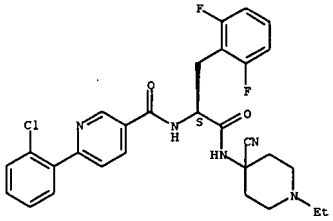
AB The dipeptide derivs. [I [R1 = substituted Ph, aryl, diaryl, heterodiaryl, furanyl, arylfuranyl, pyrazolyl, etc.; R2 = H, (un)substituted cycloalkyl, indolyl, alkylindolyl, Me, Et, Pr, pentyl, etc.; R3 = H, or R2 and R3 together with the carbon atom to which they are attached formed (un)substituted cycloalkylene, cycloalkenylene or spirocycloalkylene; R4 = H; R5 = H, (un)substituted alkyl or heteroaryl, or R4 and R5 together with the carbon atom to which they are attached form cycloalkylene or heterocycloalkylene]] were prepared as cysteine protease inhibitors, in particular, cathepsins B, K, L, F, and S, for treating diseases mediated by these proteases. Thus, compound II was prepared via peptide coupling of 2'-chlorobiphenyl-4-carboxylic acid with synthesized 2(S)-amino-N-cyanomethyl-3-(2,6-difluoro-4-methoxyphenyl)-propionamide. Compds. of the invention were tested by in vitro essays for protease activity and showed cathepsins B, K, L, F, and S inhibitory activity.

IT 710350-09-7P 710350-41-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dipeptide cyanomethyl derivs. as cysteine protease inhibitors)

RN 710350-09-7 CAPLUS
CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S)-2-[(4-cyano-1-ethyl-4-piperidinyl)amino]-1-[(2,6-difluorophenyl)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

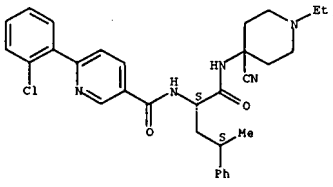
Absolute stereochemistry.

L6 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 710350-41-7 CAPLUS
CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S,3S)-1-[[(4-cyano-1-ethyl-4-piperidinyl)amino]carbonyl]-3-phenylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:208265 CAPLUS
DOCUMENT NUMBER: 134:252348
TITLE: Novel spiroheterocyclic compounds [morpholine-4-carboxylic acid amides of heterocyclic cyclohexylalanine and neopentylglycine derivatives and their analogs], useful as reversible inhibitors of cysteine proteases such as cathepsin S
INVENTOR(S): Emmanuel, Michel J.; Frye, Leah L.; Hickey, Eugene R.; Liu, Weimin; Morwick, Tina M.; Spero, Denice M.; Sun, Sanxing; Thomson, David S.; Ward, Yancey D.; Young, Erick R. R.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 361 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019816	A1	20010322	WO 2000-US23584	20000828
W: AE, AU, BG, BR, BY, CA, CN, CZ, EE, HR, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2385130	A1	20010322	CA 2000-2385130	20000828
AU 200070818	A	20010417	AU 2000-70818	20000828
AU 782246	B2	20050714		
EP 1218372	A1	20020703	EP 2000-959506	20000828
EP 1218372	B1	20030702		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
AT 244235	T	20030715	AT 2000-959506	20000828
JP 2003529546	T	20031007	JP 2001-523393	20000828
PT 1218372	T	20031128	PT 2000-959506	20000828
EE 200200132	A	20031215	EE 2002-132	20000828
ES 2199856	T3	20040301	ES 2000-959506	20000828
HU 200302380	A2	20040301	HU 2003-2380	20000828
BR 2000013966	A	20040615	BR 2000-13966	20000828
NZ 518255	A	20041126	NZ 2000-518255	20000828
RU 2255937	C2	20050710	RU 2002-107433	20000828
TW 230159	B	20050401	TW 2000-89118587	20000911
US 2002058809	A1	20020516	US 2001-1134	20011102
US 6756372	B2	20040629		
BG 106483	A	20021031	BG 2002-106483	20020305
ZA 2002001987	A	20040416	ZA 2002-1987	20020311
NO 2002001207	A	20020312	NO 2002-1207	20020312
HR 2002000221	B1	20070131	HR 2002-221	20020312
US 2003225271	A1	20031204	US 2003-422471	20030424
US 7056915	B2	20060606		
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US 6982272	B2	20060103		
US 2005032792	A1	20050210	US 2004-937533	20040909
US 2005032772	A1	20050210	US 2004-937636	20040909

PRIORITY APPLN. INFO.:

US 1999-153738P	P	19990913
US 2000-222900P	P	20000803
WO 2000-US23584	W	20000828
US 2000-655351	A3	20000908
US 2001-1134	A3	20011102
US 2003-422471	A1	20030424

OTHER SOURCE(S): MARPAT 134:252348
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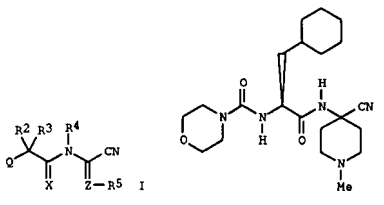


I II

AB Compds. of formula I are claimed [wherein; Q is R1C(=Y)NR4- or R1C(=NR6)NR4- or R1YNR4- or R1C(NR6R8)=N-, where R1 is (cyclo)alkyl(sulfonyl), alkoxy, aryl(sulfonyl) or hetero(aryl)(cyclyl); R2 is H or alkyl; R3 is H, (un)substituted (cyclo)alkyl, alkylene or aryl(alkyl); or R2R3 may form nonarom. carbo- or heterocyclic ring; R4 is H, OH, or alkyl; R5 is bond, H, alkyl optionally interrupted by 1 or 2 O, S, Ph, naphthyl, heterocyclyl, etc.; R6 is H, OH, CN, etc.; R8 is alkyl optionally interrupted by N, O, S, etc.; X, Y are O or S; Z is a spirocyclic junction to certain 4-7 membered ring (substituted)(bridged)(fused)heterocycles]. The compds. are novel, reversible inhibitors of cathepsins S, K, F, L and B, and are useful for treating a variety of autoimmune diseases. Also disclosed are processes for preparing I. Over 100 examples, primarily derived from L-cyclohexylalanine and L-neopentylglycine, are given. Claims cover the same compds. with unspecified stereochem. For example, L-β-cyclohexylalanine Me ester hydrochloride was neutralized, amidated with 4-morpholinecarbonyl chloride, and saponified with LiOH in aqueous MeOH-THF to give N-(4-morpholinecarbonyl)-L-cyclohexylalanine. This acid derivative was coupled with crude 4-amino-4-cyano-1-methylpiperidine using EDC in the presence of HOBT and N-methylmorpholine in DMF, yielding title compound II. Compds. I inhibited human recombinant cathepsin S in vitro with IC50 values of 100 μM or below.

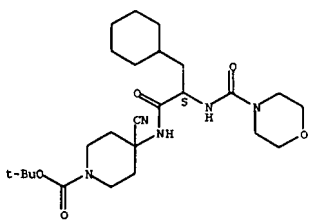
IT 331278-93-4P, (S)-4-Cyano-4-[3-cyclohexyl-2-[(morpholine-4-carbonyl)amino]propionylamino]piperidine-1-carboxylic acid tert-butyl ester 331278-94-5P, (S)-Morpholine-4-carboxylic acid [1-(4-cyanopiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of spiroheterocyclic morpholine derivs. of cyclohexylalanine and neopentylglycine as reversible inhibitors of cysteine proteases)

RN 331278-93-4 CAPLUS

L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-3-cyclohexyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopropyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

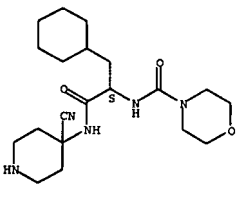
Absolute stereochemistry.



RN 331278-94-5 CAPLUS

CN 4-Morpholinecarboxamide, N-[(1S)-2-[(4-cyano-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT 331278-68-3P, (S)-Morpholine-4-carboxylic acid [1-(4-cyano-1-methylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331278-70-7P, (S)-4-Cyano-4-[3-cyclohexyl-2-[(morpholine-4-carbonyl)amino]propionylamino]piperidine-1-carboxylic acid ethyl ester 331278-71-8P, (S)-Morpholine-4-carboxylic acid [1-(4-cyano-1-phenethylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331278-72-9P, (S)-Morpholine-4-carboxylic acid [1-(1-benzyl-4-cyanopiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331278-73-0P, (S)-Morpholine-4-carboxylic acid [1-(4-cyano-1-propylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331278-74-1P, (S)-4-Cyano-4-[3-cyclohexyl-2-[(morpholine-4-carbonyl)amino]propionylamino]piperidine-1-carboxylic acid benzyl ester

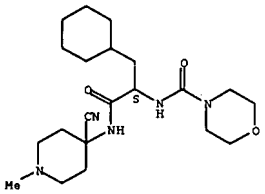
L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

331278-76-3P, (S)-Morpholine-4-carboxylic acid [1-(4-cyano-1-pyrimidin-2-ylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331278-77-4P, (S)-Morpholine-4-carboxylic acid [1-(1-acetyl-4-cyanopiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331278-80-9P, (S)-Morpholine-4-carboxylic acid [1-(1-benzyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331278-81-0P, (S)-Morpholine-4-carboxylic acid [1-(1-isopropyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331278-82-1P, (S)-Morpholine-4-carboxylic acid [1-(1-phenethyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331278-83-2P, (S)-Morpholine-4-carboxylic acid [1-(1-n-propyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331278-84-3P, (S)-4-Cyano-4-[4,4-dimethyl-2-[(morpholine-4-carbonyl)amino]pentanoylamino]piperidine-1-carboxylic acid benzyl ester 331278-85-4P, (S)-Morpholine-4-carboxylic acid [1-(1-acetyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331278-86-5P, (S)-Morpholine-4-carboxylic acid [1-(1-benzoyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331278-87-6P, (S)-4-Cyano-4-[4,4-dimethyl-2-[(morpholine-4-carbonyl)amino]pentanoylamino]piperidine-1-carboxylic acid ethyl ester 331278-88-7P, (S)-Morpholine-4-carboxylic acid [1-[4-cyano-1-(2-dimethylaminoacetyl)piperidin-4-ylcarbamoyl]-2-cyclohexylethyl]amide 331278-90-1P, (S)-Morpholine-4-carboxylic acid [1-(4-cyano-1-methylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331278-95-6P, (S)-Morpholine-4-carboxylic acid [1-[4-cyano-1-(1-methylethyl)piperidin-4-ylcarbamoyl]-2-cyclohexylethyl]amide 331278-97-8P 331279-07-3P, (S)-Morpholine-4-carboxylic acid [1-(1-carbamimidoyl-4-cyanopiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide p-toluenesulfonate 331279-08-4P, (S)-Morpholine-4-carboxylic acid [1-(4-cyano-1-phenylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331279-09-5P, (S)-Morpholine-4-carboxylic acid [1-(1-tert-butyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331279-10-8P, (S,S)-Morpholine-4-carboxylic acid [1-(4-cyano-1,2-dimethylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331279-11-9P, (S)-Morpholine-4-carboxylic acid [1-(4-cyano-1-cyclohexylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331279-12-0P, (S)-Morpholine-4-carboxylic acid [1-[4-cyano-1-(tetrahydropyran-4-yl]piperidin-4-ylcarbamoyl]-3,3-dimethylbutyl]amide 331279-58-4P, (S)-Morpholine-4-carboxylic acid [1-[4-cyano-1-(1-methylpiperidine-4-carbonyl)piperidin-4-ylcarbamoyl]-2-cyclohexylethyl]amide 331279-59-5P, (S)-Morpholine-4-carboxylic acid [1-[4-cyano-1-(pyridine-4-carbonyl)piperidin-4-ylcarbamoyl]-2-cyclohexylethyl]amide 331279-68-6P, (S)-4-Cyano-4-[3-cyclohexyl-2-[(piperidine-4-carbonyl)amino]propionylamino]piperidine-1-carboxylic acid ethyl ester 331279-69-7P, (S)-4-Cyano-4-[3-cyclohexyl-2-[(4-methylpiperazine-1-carbonyl)amino]propionylamino]piperidine-1-carboxylic acid ethyl ester 331280-11-6P, Morpholine-4-carboxylic acid [1-[4-cyano-1-methylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331280-14-9P, Morpholine-4-carboxylic acid [1-(4-cyano-1-methylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331280-15-0P, Morpholine-4-carboxylic acid [1-(1-benzyl-4-cyanopiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331280-16-1P, Morpholine-4-carboxylic acid [1-(4-cyanopiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide hydrochloride 331280-17-2P, Morpholine-4-carboxylic acid [1-[4-cyano-1-(1-methylethyl)piperidin-4-ylcarbamoyl]-2-cyclohexylethyl]amide 331280-18-3P, Morpholine-4-carboxylic acid [1-(4-cyano-1-phenethylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331280-20-7P,

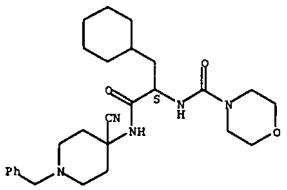
L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Morpholine-4-carboxylic acid [1-(4-cyano-1-propylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331280-21-8P, Morpholine-4-carboxylic acid [1-(4-cyano-1-isopropylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331280-22-9P, Morpholine-4-carboxylic acid [1-(1-phenethyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331280-23-0P, Morpholine-4-carboxylic acid [1-(1-n-propyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331280-24-1P , Morpholine-4-carboxylic acid [1-(1-benzyl-4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331280-30-9P, N-[1-(4-Cyano-1-methylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]isonicotinamide 331280-31-0P, Pyrazine-2-carboxylic acid [1-(4-cyano-1-methylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331280-32-1P, 5-Chlorothiophene-2-carboxylic acid [1-(4-cyano-1-methylpiperidin-4-ylcarbamoyl)-2-cyclohexylethyl]amide 331280-80-9P, Pyrazine-2-carboxylic acid [1-(4-cyano-1-propylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331280-83-2P, Morpholine-4-carboxylic acid [1-(4-cyano-1-cyclohexylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331280-84-3P, Morpholine-4-carboxylic acid [2-(4-chlorophenyl)-1-(4-cyano-1-propylpiperidin-4-ylcarbamoyl)ethyl]amide 331280-85-4P , Morpholine-4-carboxylic acid [1-(4-cyano-1-propylpiperidin-4-ylcarbamoyl)-2-(3,4-dichlorophenyl)ethyl]amide 331280-86-5P, Morpholine-4-carboxylic acid [1-(4-cyano-1-propylpiperidin-4-ylcarbamoyl)-2-naphthalen-2-ylethyl]amide 331280-87-6P, Morpholine-4-carboxylic acid [1-(4-cyano-1-propylpiperidin-4-ylcarbamoyl)-3-methylbutyl]amide 331280-88-7P, Morpholine-4-carboxylic acid [1-(4-cyano-1,2-dimethylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331281-53-9P, (S,R)-Morpholine-4-carboxylic acid [1-(4-cyano-1,2-dimethylpiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide 331444-07-6P 331444-09-8P 331444-11-2P 331444-12-3P, (S)-Morpholine-4-carboxylic acid [1-(3-cyano-8-methyl-8-azabicyclo[3.2.1]oct-3-ylcarbamoyl)-2-cyclohexylethyl]amide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of spiroheterocyclic morpholine derivs. of cyclohexylalanine and neopentylglycine as reversible inhibitors of cysteine proteases)

RN 331278-68-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

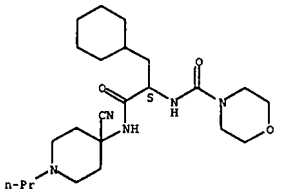


L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



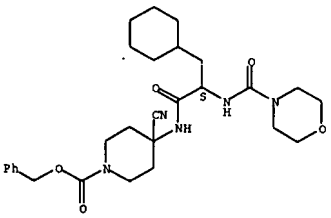
RN 331278-73-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(4-cyano-1-propyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



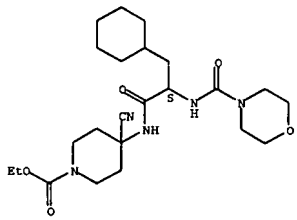
RN 331278-74-1 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-3-cyclohexyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopropyl]amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



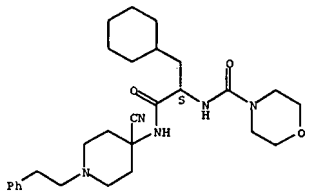
L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 331278-70-7 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-3-cyclohexyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopropyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331278-71-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[4-cyano-1-(2-phenylethyl)-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



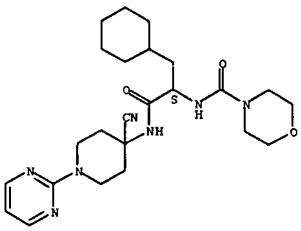
RN 331278-72-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[4-cyano-1-(phenylmethyl)-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

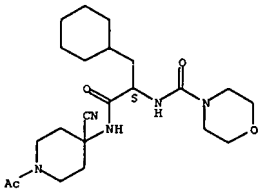
RN 331278-76-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[4-cyano-1-(2-pyrimidinyl)-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



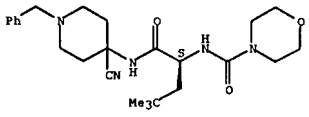
RN 331278-77-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(1-acetyl-4-cyano-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



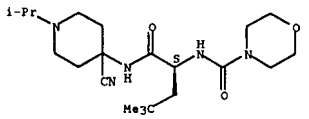
RN 331278-80-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(phenylmethyl)-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



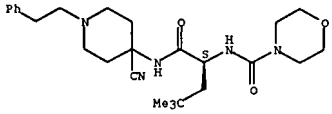
RN 331278-81-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(1-methylethyl)-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



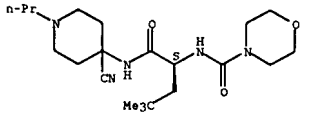
RN 331278-82-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(2-phenylethyl)-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

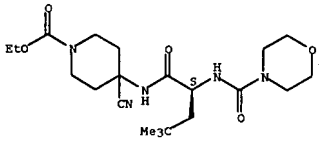


RN 331278-83-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-propyl-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

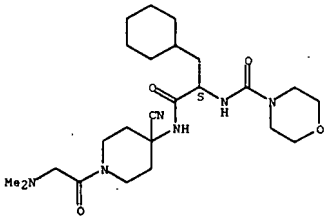


RN 331278-84-3 CAPLUS



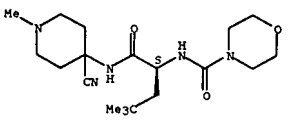
RN 331278-88-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[4-cyano-1-[(dimethylamino)acetyl]-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331278-90-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

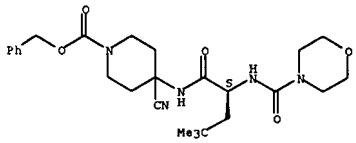


RN 331278-95-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[4-cyano-1-(1-methylethyl)-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

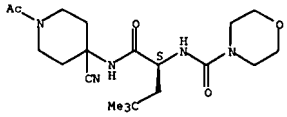
CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-4,4-dimethyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



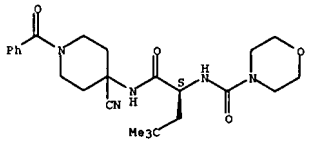
RN 331278-85-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(1-acetyl-4-cyano-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



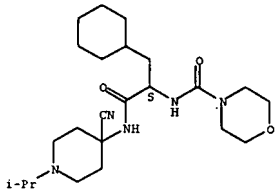
RN 331278-86-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(1-benzoyl-4-cyano-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



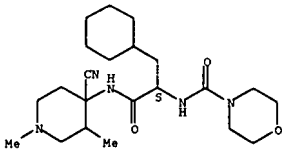
RN 331278-87-6 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-4,4-dimethyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331278-97-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(4-cyano-1,3-dimethyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

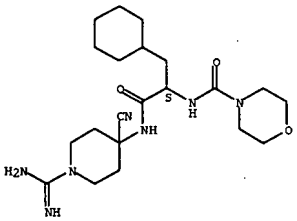


RN 331279-07-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[1-(aminoiminomethyl)-4-cyano-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

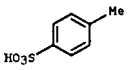
CRN 331279-06-2
CMF C21 H35 N7 O3

Absolute stereochemistry.



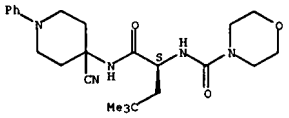
CM 2

CRN 104-15-4
CMF C7 H8 O3 S



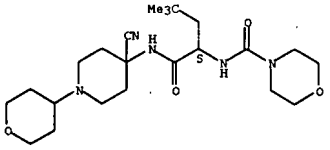
RN 331279-08-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-phenyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



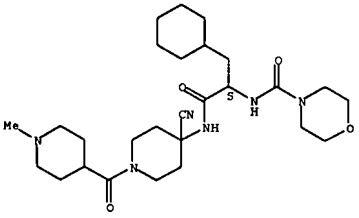
RN 331279-09-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(1,1-dimethylethyl)-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



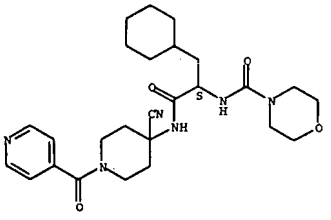
RN 331279-58-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[4-cyano-1-[(1-methyl-4-piperidinyl)carbonyl]-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

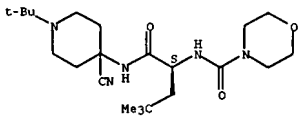
Absolute stereochemistry.



RN 331279-59-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[4-cyano-1-(4-pyridinylcarbonyl)-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

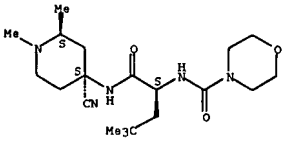
Absolute stereochemistry.





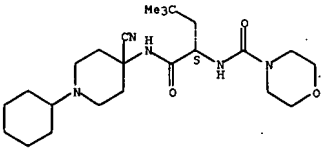
RN 331279-10-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(2S,4S)-4-cyano-1,2-dimethyl-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331279-11-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-1-cyclohexyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

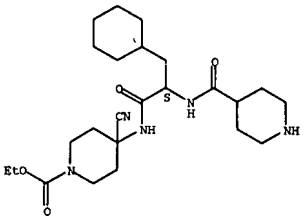


RN 331279-12-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[4-cyano-1-(tetrahydro-2H-pyran-4-yl)-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

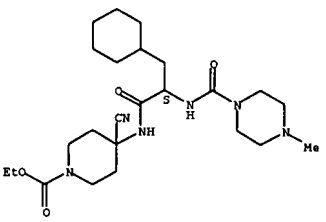
RN 331279-68-6 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-3-cyclohexyl-1-oxo-2-[(4-piperidinylcarbonyl)amino]propyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

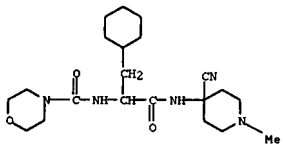


RN 331279-69-7 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-3-cyclohexyl-2-[[(4-methyl-1-piperazinyl)carbonyl]amino]-1-oxopropyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

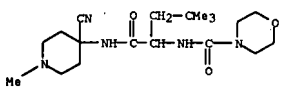
Absolute stereochemistry.



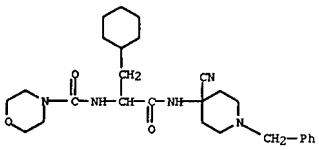
RN 331280-11-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



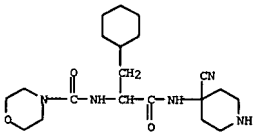
RN 331280-14-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



RN 331280-15-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[[4-cyano-1-(phenylmethyl)-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

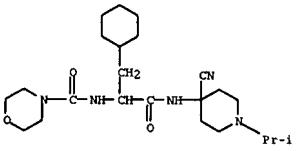


RN 331280-16-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(4-cyano-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

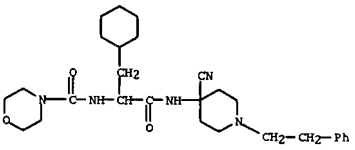


● HCl

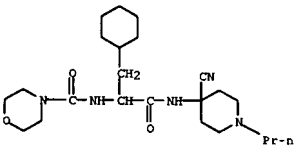
RN 331280-17-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[[4-cyano-1-(1-methylethyl)-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



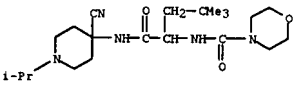
RN 331280-18-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[[4-cyano-1-(2-phenylethyl)-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



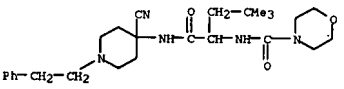
RN 331280-20-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(4-cyano-1-propyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



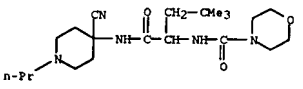
RN 331280-21-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[[4-cyano-1-(1-methylethyl)-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



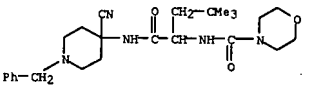
RN 331280-22-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[[4-cyano-1-(2-phenylethyl)-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



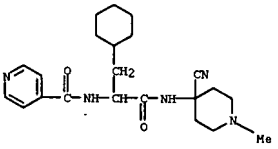
RN 331280-23-0 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



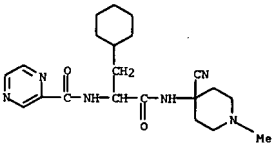
RN 331280-24-1 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[[4-cyano-1-(phenylmethyl)-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



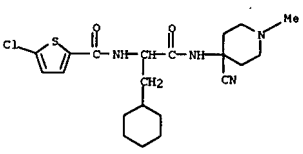
RN 331280-30-9 CAPLUS
CN 4-Pyridinecarboxamide, N-[2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 331280-31-0 CAPLUS
CN Pyrazinecarboxamide, N-[2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

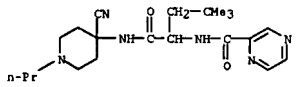


RN 331280-32-1 CAPLUS
CN 2-Thiophenecarboxamide, 5-chloro-N-[2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

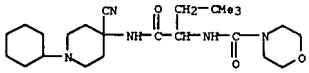


L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

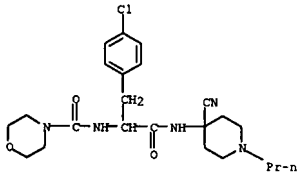
RN 331280-80-9 CAPLUS
CN Pyrazinecarboxamide, N-[1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



RN 331280-83-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-cyclohexyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

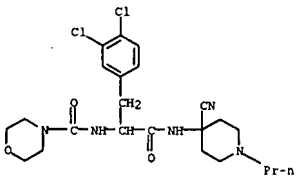


RN 331280-84-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[(4-chlorophenyl)methyl]-2-[(4-cyano-1-propyl-4-piperidinyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

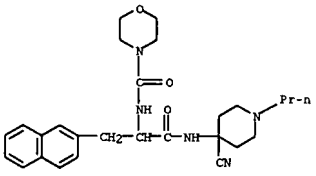


RN 331280-85-4 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(4-cyano-1-propyl-4-piperidinyl)amino]-1-[(3,4-dichlorophenyl)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

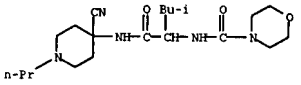
L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



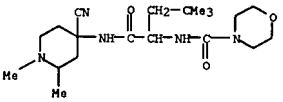
RN 331280-86-5 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[(4-cyano-1-propyl-4-piperidinyl)amino]-1-(2-naphthalenylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 331280-87-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]-3-methylbutyl]- (9CI) (CA INDEX NAME)



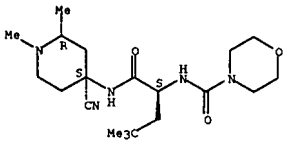
RN 331280-88-7 CAPLUS
CN 4-Morpholinecarboxamide, N-[1-[[(4-cyano-1,2-dimethyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

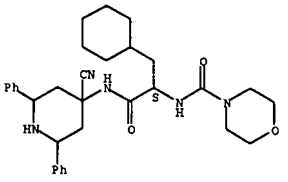
RN 331281-53-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[[(2R,4S)-4-cyano-1,2-dimethyl-4-piperidinyl]amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



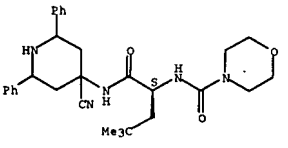
RN 331444-07-6 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(4-cyano-2,6-diphenyl-4-piperidinyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331444-09-8 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-2,6-diphenyl-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

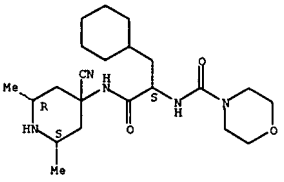


RN 331444-11-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[[(2α,6α)-4-cyano-2,6-

L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

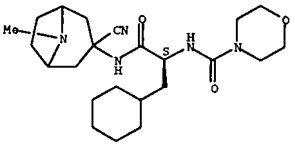
dimethyl-4-piperidinyl]amino]-1-(cyclohexylmethyl)-2-oxoethyl]-, rel- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331444-12-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-2-[(3-cyano-8-methyl-8-azabicyclo[3.2.1]oct-3-yl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

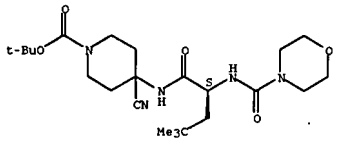


IT 331281-29-9P, (S)-4-Cyano-4-[4,4-dimethyl-2-[(morpholine-4-carbonyl)amino]pentanoylamino]piperidine-1-carboxylic acid tert-butyl ester 331281-30-2P, (S)-Morpholine-4-carboxylic acid [1-(4-cyanopiperidin-4-ylcarbamoyl)-3,3-dimethylbutyl]amide hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of spiroheterocyclic morpholine derivs. of cyclohexylalanine and neopentylglycine as reversible inhibitors of cysteine proteases)

RN 331281-29-9 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-4,4-dimethyl-2-[(4-morpholinylcarbonyl)amino]-1-oxopentyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

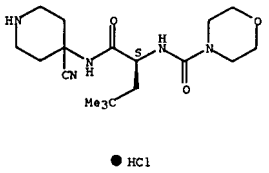
Absolute stereochemistry.

L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 331281-30-2 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1S)-1-[[(4-cyano-4-piperidinyl)amino]carbonyl]-3,3-dimethylbutyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

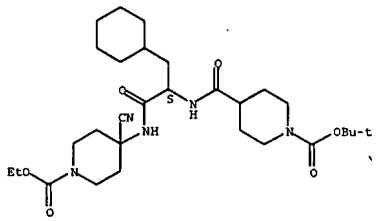


● HCl

IT 331281-36-8, (S)-4-Cyano-4-[3-cyclohexyl-2-[(1-t-butoxycarbonylpiperidine-4-carbonyl)amino]propionylamino]piperidine-1-carboxylic acid ethyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; preparation of spiroheterocyclic morpholine derivs. of cyclohexylalanine and neopentylglycine as reversible inhibitors of cysteine proteases)
RN 331281-36-8 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-cyano-4-[[(2S)-3-cyclohexyl-2-[[[1-[(1,1-dimethylethoxy)carbonyl]-4-piperidinyl]carbonyl]amino]-1-oxopropyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L6 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



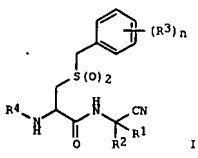
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

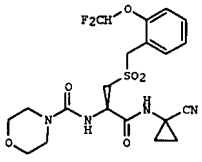
ACCESSION NUMBER: 2001:208258 CAPLUS
DOCUMENT NUMBER: 134:237310
TITLE: Preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivatives as as cathepsin S inhibitors
INVENTOR(S): Graupe, Michael; Link, John O.; Patterson, John W.; Zipfel, Sheila
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001019808	A1	20010322	WO 2000-US25341		20000915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6492362	B1	20021210	US 2000-663449		20000915
US 2004014796	A1	20040122	US 2002-256354		20020927
PRIORITY APPLN. INFO.:			US 1999-154245P	P	19990916
			US 1999-171831P	P	19991222
			US 2000-224552P	P	20000810
			US 2000-663449	A3	20000915

OTHER SOURCE(S): MARPAT 134:237310
GI



I

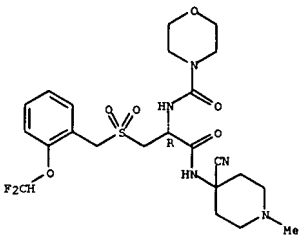


II

AB Compds. of formula I are claimed (wherein; n is 1-5, R1 is H and R2 is cyano, C5-heteroaryl or R1 and R2 are H, halo, alkyl, alkyl, X1OR5 where X1 and R5 are defined below or R1 and R2 together with the carbon atom, are (hetero)cycloalkylene; R3 is, at the first occurrence, NO2, CF3O, CHF2O, X1NR5R5, X1C(O)NR5R5, X1SR5, etc., where X1 is a bond or alkylene, R5 is H or (substituted)alkyl; R3 is at each other occurrence, is H, alkyl, CN, halo, etc.; R4 is C(O)X2R8 or S(O)2X2R8, where X2 is a bond, O or N(H or alkyl) and R8 is (substituted)alkyl, (hetero)cycloalkyl, substituted heteroaryl, etc.]. Prepn. of I proceeds by one of four routes. The cyanomethyl amide side-chain may be formed by condensation of a cyanomethylamine with the parent carboxylic acid (optionally as the sulfide analog, followed by oxidn. to the sulfone). The R4-NH bond may be formed by alkylation of the parent amine salt with R4L where L is a leaving group, or by addn. of an amine to the corresponding isocyanate. Alternatively, the thiol-derived parent may be S-benzylated and oxidized to give compds. I. Compd. II was prepd. by amidation of (R)-3-[2-(difluoromethoxy)benzylsulfonyl]-2-[(1-morpholin-4-ylmethanoyl)amino]propionic acid with (1-aminocyclopropane)carbonitrile. Seventy examples of compds. I were provided. I showed Ki against cathepsin S activity in the range of 10-10 to 10-7 M. I inhibited cathepsin K 50-fold less than cathepsin S. Claimed uses of I are treatment of diseases which inhibition of cathepsin S can prevent.

IT 330474-82-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivs. as selective cathepsin S inhibitors)
RN 330474-82-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:208246 CAPLUS
DOCUMENT NUMBER: 134:237830
TITLE: Preparation of amino acid cyanomethyl amides as cathepsin S inhibitors
INVENTOR(S): Graupe, Michael; Link, John O.; Patterson, John W.; Zipfel, Sheila
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 261 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019796	A1	20010322	WO 2000-US25415	20000915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2384974	A1	20010322	CA 2000-2384974	20000915
EP 1212302	A1	20020612	EP 2000-966734	20000915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6492362	B1	20021210	US 2000-663449	20000915
JP 2003509410	T	20030311	JP 2001-523376	20000915
AU 777472	B2	20041021	AU 2000-77033	20000915
US 2004014796	A1	20040122	US 2002-256354	20020927

PRIORITY APPLN. INFO.:

US 1999-154245P	P	19990916
US 1999-171831P	P	19991222
US 2000-224552P	P	20000810
US 2000-663449	A3	20000915
WO 2000-US25415	W	20000915

OTHER SOURCE(S): MARPAT 134:237830

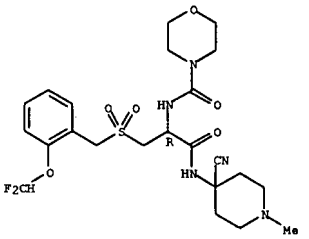
AB R4NHCH(X1SO2X2R3)CONHCR1R2CN [X1, X2 = CH2, or X1 = CH2CH2 and X2 = bond; R1 = H, R2 = cyano, heteroaryl, alkylheteroaryl, or R1, R2 = H, halo, alkyl, X3OR9; R1R2C = cycloalkylene, heterocycloalkylene; R3 = (substituted) CHR5:CHR6, CR7:NR8; R5R6 = atoms to form alkenyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, etc.; R7R8 = atoms to form heterocycloalkenyl, heteroaryl, heterobicycloaryl; R4 = COX4R11, SO2X4R11; X4 = bond, O, NR12; R12 = H, alkyl; R11 = (substituted) alkyl, cycloalkylalkyl, heterocycloalkylalkyl, etc.; R9 = H, alkyl, haloalkyl; X3 = bond, alkylene], were prepared Thus, 2R-benzoylamino-3-(4-methylbenzylsulfanyl)propionic acid (preparation given), EDCI, HOBt, aminoacetonitrile bisulfate, and N-methylmorpholine were stirred together in N-methylpyrrolidinone for 5 h to give N-[1R-cyanomethylcarbamoyl-2-(4-methylbenzylsulfanyl)ethyl]benzamide. This was stirred with oxone in MeOH for 16 h to give N-[(R)-1-(cyanomethylcarbamoyl)-2-p-tolylmethanesulfonylethyl]benzamide. Title compds. inhibited cathepsin S with Ki = about 10-10 M to 10-4 M.

IT 330474-82-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L6 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(prepn. of amino acid cyanomethyl amides as cathepsin S inhibitors)

RN 330474-82-3 CAPLUS
CN 4-Morpholinecarboxamide, N-[(1R)-2-[(4-cyano-1-methyl-4-piperidinyl)amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT